~~28~~ 106. (New) A method according to claim ~~23~~ 1, wherein the nucleotide is a constituent of a DNA or RNA polynucleotide.

REMARKS

Claims 23, 30, 32, 34, 35, and 49 have been amended. Claim 46 has been cancelled. Claims 51-105 were withdrawn from consideration in Applicants' amendment dated July 23, 2001. These claims have now been cancelled. Claim 106 has been added. Accordingly, claims 23-45, 47-50 and 106 are pending in this application. Reconsideration is respectfully requested.

Applicants wish to thank Examiner Sisson for conducting an interview with their representative, the undersigned, at the Patent and Trademark Office on August 9, 2001. A representative of the assignee, Jack Veuskens, was present at the interview. The courtesy shown by Examiner Sisson to applicants' representatives as well as his cooperation and assistance in drafting patentable claims are especially appreciated.

Applicants further wish to thank Examiner Sisson for further discussing claim language with their representative on September 6, 2001. Applicants deeply appreciate Examiner Sisson's diligence in improving the claim language. The claims have been amended to reflect the agreements reached during the August 9 and September 6 discussions.

Examiner Sisson pointed out during the discussion on September 6 that the supplemental amendment submitted on August 17, 2001 would not be entered, since an extension of time had not been requested. Accordingly, the present supplemental amendment is the only supplemental amendment of record. Examiner Sisson stated, and applicants' representative agreed, that an extension of time of two months is required. A request for a two month extension of time is enclosed herewith.

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The following remarks summarize the discussions of August 9 and September 6, 2001.

During the August 9, 2001 interview, applicants' representative reviewed the rejection in the office action dated March 22, 2001, and applicants' response to the office action in their amendment dated July 23, 2001. Examiner Sisson indicated that he understood the response.

Examiner Sisson then stated that, upon reviewing the claims, he considered a final issue to relate to the breadth of the term "spacer" in claim 23. Examiner Sisson stated that the term did not have an upper limit on the number of atoms in the spacer. Applicants' representative stated that a person having ordinary skill in the art would have no difficulty ascertaining the size of the spacer in view of the totality of the disclosure in the specification.

Applicants and their representatives particularly appreciate the suggestion made by Examiner Sisson. In particular, Examiner Sisson suggested the term "spacer means," thereby invoking the provisions of 35 U.S.C. §112, paragraph 6.

In order to expedite the prosecution, applicants have accepted the examiner's suggestion. The claims have been amended accordingly. As stated by the examiner in the interview summary, "...the disclosure had been found to set forth a variety of suitable spacers and as such, the claim would be limited to those spacers disclosed and the equivalents thereof; 35 U.S.C. §112, paragraph 6." The "variety of suitable spacers" may be found throughout the specification, for example, the spacers encompassed by the disclosure at page 4, line 28 to page 7, line 3.

Claim 23 has been further amended, claims 46 cancelled, and claim 106 added, all in accordance with agreements reached during the September 6, 2001 discussion.

This application is now believed to be in condition for allowance. Notice to that effect at the examiner's earliest convenience is respectfully requested.

Respectfully submitted,

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VERSION OF AMENDMENT WITH MARKINGS TO SHOW CHANGES MADE

Cancel claims 1-22 and claim 46. Amend claims 23-50 and add new claim 106.

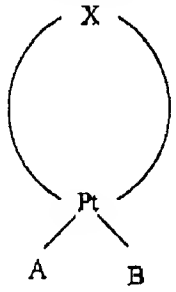
23. (Amended) A method for labeling a nucleotide comprising:

providing a label;

providing a spacer means comprising ~~a chain having at least four atoms,~~ a spacer reactive moiety at one end ~~of the chain,~~ and an electron donating moiety at the other end of the ~~chain~~ spacer means, wherein the spacer reactive moiety is capable of coupling the spacer means to a label when the spacer reactive moiety is reacted with the label;

providing a nucleotide;

providing a linker having formula I,



(I)

wherein X represents an aliphatic diamine, and A and B represent the same or different linker reactive moieties capable of reacting with the electron donating group of the spacer means or with the nucleotide, thereby attaching the spacer means or the nucleotide to the linker;

reacting the spacer reactive moiety with the label, thereby coupling the spacer means to the label;

reacting the electron donating moiety of the spacer means with one of the linker reactive moieties, thereby attaching the spacer means to the linker; and

reacting the nucleotide with the other linker reactive moiety, thereby attaching the nucleotide to the linker.

24. The method according to claim 23, wherein X represents an aliphatic diamine having 2-6 carbon atoms.

25. The method according to claim 23, wherein X represents an aliphatic diamine having the formula $G_2NCH_2\ CH_2\ NG_2$, wherein G represents H or an alkyl group of from 1 to 6 carbon atoms.

26. The method according to claim 23, wherein X represents ethylenediamine.

27. The method according to claim 23, wherein X represents N,N,N',N'-tetramethylethylenediamine.

28. The method according to claim 23, wherein A and B represent NO_3^-, SO_3^-, Cl^-, I^-, other halogen or Me_2SO.

29. The method according to claim 23, wherein A and B are the same.

30. (Amended) The method according to claim 23, wherein the spacer means comprises no more than twenty carbon atoms.

31. The method according to claim 30, wherein the carbon atoms are non-branched.

32. (Amended) The method according to claim 23, wherein the spacer means comprises four carbon atoms and one heteroatom.

33. The method according to claim 32, wherein the heteroatom is oxygen.

34. (Amended) The method according to claim 23, wherein the spacer means is 1,8-diamino-3,6-dioxaoctane.

35. (Amended) The method according to claim 23, wherein the spacer means is an oligolysine or a polylysine.

36. The method according to claim 23, wherein the electron donating moiety is an amino group or a thiolate group.

37. The method according to claim 36, wherein the amino group is an aromatic amino group.

38. The method according to claim 36, wherein the amino group is an imidazole or purine group.

39. The method according to claim 23, wherein the spacer reactive moiety is NH_2.

40. The method according to claim 23, wherein the label is radioactive.

41. The method according to claim 23, wherein the label is an enzyme.

42. The method according to claim 23, wherein the label is a component of a specific binding pair.

43. The method according to claim 23, wherein the specific binding pair is biotin and avidin or streptavidin.

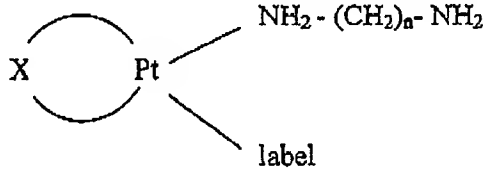
44. The method according to claim 23, wherein the label is a dye, a fluorochrome, or a reducing agent.

45. The method according to claim 23, wherein the label is digoxygenin.

47. The method according to claim 23, wherein the nucleotide is adenine, thymidine, cytosine, and either guanine or uridine.

48. The method according to claim 23, wherein the nucleotide is a purine.

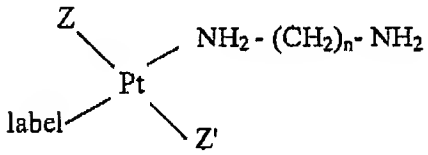
49. The method according to claim 23 wherein the linker is reacted with a labeling moeity comprising



(II)

structure corrected

or the formula



(III)

wherein X represents an aliphatic diamine, Z and Z' represent a non-leaving ligand and n is an integer of from 2 to 10.

50. A method according to claim 49, wherein Z and/or Z' represent an NH_3, NH_2R, NHR_2, or NR_3 group, wherein R represents an alkyl group having from 1 to 6 carbon atoms.

106. (New) A method according to claim 23, wherein the nucleotide is a constituent of a DNA or RNA polynucleotide.